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DOI: <https://doi.org/10.1007/s00415-007-0531-x>

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ZORA URL: <https://doi.org/10.5167/uzh-95586>

Journal Article

Published Version

Originally published at:

Poryazova, R; Schnepf, B; Boesiger, P; Bassetti, C L (2007). Magnetic resonance spectroscopy in a patient with Kleine-Levin syndrome. *Journal of Neurology*, 254(10):1445-1446.

DOI: <https://doi.org/10.1007/s00415-007-0531-x>

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Magnetic resonance spectroscopy in a patient with Kleine-Levin syndrome

Received: 18 September 2006
Received in revised form:
29 December 2006
Accepted: 16 January 2007
Published online: 15 October 2007

Sirs: Kleine-Levin syndrome (KLS) is a rare recurrent hypersomnia associated with behavioural, cognitive, eating and sexual disturbances [1, 2]. A recent SPECT study in 7 patients with (KLS) showed decreased thalamic perfusion during the hypersomnolent attacks [3]. These findings were later confirmed in a case report by Hong et al. [4]. Proton magnetic resonance spectroscopy (^1H MRS) is a noninvasive method of obtaining metabolic information. By means of MRS, different compounds can be measured including N-acetylaspartate (NAA), a marker of neuronal integrity and glutamate-glutamine (Glu-Gln), which plays an important role in excitatory neurotransmission and mitochondrial metabolism [5].

We present a 19-year-old patient with idiopathic, classical KLS. Over

a 4-year period he suffered 19 stereotypical hypersomnolent episodes. The attacks were always preceded or accompanied by fever up to 39 °C, sore throat or stomach pain. At the beginning of the episodes mood depression was observed, the patient was melancholic, sad and withdrew socially. Sleep behaviour reached 20 hours/day, interrupted by compulsive eating, 7–8/days without any specific food preference resulting in a weight gain of approximately 5 kg/attack. Sexual disinhibition with masturbation, irritability, aggressiveness, cognitive and concentration disturbances were frequent. The attacks usually ended with insomnia lasting 2–3 days and a subsequent gradual improvement of emotional state and cognition. The patient described this phase as awakening from a dream and had difficulty recalling the events that had occurred during the attack. In the first year before treatment 12 attacks were observed. Under therapy with lithium 30 mg/day and valproic acid 2000 mg/day a remarkable reduction in frequency and severity of the episodes (7 attacks over a period of 2.5 years) was noted. The duration of the hypersomnolent episodes remained unchanged, 10 days on average.

Hypocretin-1 in the cerebrospinal fluid during an attack was in the normal range, 530 pg/ml.

The patient underwent ^1H MRS in an asymptomatic period and a month later during a typical episode. Because of presumed hypothalamic [6] or thalamic [3, 4] dysfunction in KLS we chose three regions of interest: hypothalamus and both thalami. MRS was performed on a Philips Achieva 3.0 T scanner. Single-voxel proton MR spectra, voxels of 17 x 14 x 15 mm in both thalami (3.57 cm³) and of 10 x 10 x 10 mm (1 cm³) in the hypothalamus, were acquired and

processed to determine metabolite concentration ratios. A remarkable change between the two examinations was observed in the concentration ratios of NAA-NAAG, (total NAA)/Cr and Glu-Gln/Cr (Fig. 1).

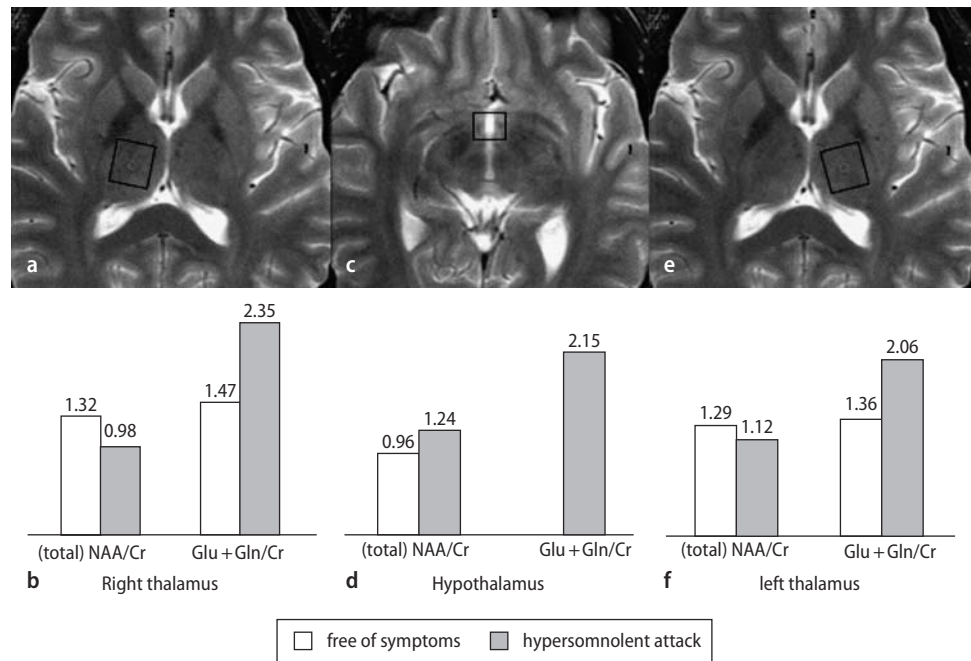
During the attack lower (total NAA)/Cr ratios in the right (–25.7 %) and left (–13.2 %) thalami were observed. In the hypothalamus the (total NAA)/Cr ratio was slightly higher in the second scan during the hypersomnolent attack. The Glu-Gln/Cr ratio was higher during the attack – in both the right (59.8 %) and left (52.3 %) thalamus. In hypothalamus a reliable value for Glu-Gln/Cr ratio was obtained only during the second scan and it was similar to the values in both thalami.

Different values for intraindividual metabolite ratio, variability and reproducibility of the results are reported in the literature, depending on the technical parameters of the acquisition and on the region of interest. For example an intraindividual temporal cortical variation up to 12 % was observed for (total NAA)/Cr and up to 29 % for Glu-Gln/Cr on a 3T scanner [7]. The decrease in the (total NAA)/Cr concentration ratio in both thalami during the hypersomnolent episode in our patient exceeds the normal range of the intraindividual variability at 3T. Our finding supports the hypothesis of a thalamic dysfunction in KLS, recently suggested by other authors [3, 4]. This hypothesis is indirectly supported also by the observation of KLS-similar symptoms (reduced alertness, impaired sleep and behavioural changes) following paramedian thalamic strokes [8]. The observed high Glu-Gln/Cr concentration ratio in all regions of interest during the episode points to additional, global metabolic changes in the brain. Glutamate is a primary excitatory neurotransmitter. Decreased NAA/Cr and increased

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Fig. 1



Glu + Gln/Cr ratios have been reported in focal epilepsies in areas without structural abnormalities, linked to ictal and interictal epileptiform activities [9] as well as in the thalamus of patients with idiopathic generalised epilepsy, possibly related to excitotoxicity [10]. The neuronal pathophysiology of epilepsy is however different from that of KLS. The remarkable increase in Glu-Gln/Cr in our patient may account for a depolarisation block and post-excitatory suppression of various thalamic nuclei. A consequence of the large cortical projections of the thalamus may be that it leads to a widespread cortical suppression. As we report a single case, a confirmation of our hypothesis is needed.

■ **Acknowledgments** Dr. Pierluigi Pedrazzi, Hospital "San Giovanni" Bellinzona who kindly referred the patient.

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